October 19, 2001

MEMORANDUM

To: Dermatologists
From: Robert Stroube, M.D., M.P.H.
Director, Office of Epidemiology
Subject: Guidelines for Evaluating Suspected Cases of Cutaneous Anthrax

Please share this memo with Primary Care Physicians, Emergency Medicine Directors, Infection Control Practitioners, Infectious Disease Physicians, and other Health Care Providers who can use the information.

We would like to provide you with some information about cutaneous anthrax, based on New York City's recent experiences. As you undoubtedly are aware, a third case of cutaneous anthrax has been identified in New York City in a 27 year old female who worked at CBS News and had primary responsibility for opening thousands of pieces of mail daily. She did not recall a specific threat letter that may have been the source of exposure. On October 1st, she noticed two small papules on her face, and over the next 24 hours developed significant facial swelling. Associated symptoms included nausea, diarrhea, sore throat, and cervical lymphadenopathy. She was treated empirically with Augmentin for 5 days for a presumed infected insect bite. After several days she developed an eschar. On October 12th, after announcement of the NBC case, the patient was reported to the New York City Department of Health and was empirically started on ciprofloxacin. A dermatology consult was obtained, and the skin biopsy was positive by immunohistochemical staining for the cell wall antigen of *B. anthracis.*

All three cases in New York City have had an association with a major news network. The first case occurred in a 38 year old female who worked for NBC News; she developed a lesion on September 25. The second case occurred in an infant whose mother worked for ABC News; he developed a skin lesion on September 29, one day after visiting his mother's office. Of note, the preliminary diagnosis for all three cases was an infected insect bite (a brown recluse spider bite was the leading diagnosis for both the first and second case), emphasizing the importance of considering anthrax in the differential diagnosis of an ulcerative or necrotic lesion, especially if associated with surrounding edema, vesicles and an eschar**.**

The small number of clinical cases resulting from confirmed or presumed exposure to envelopes contaminated with anthrax spores, suggests that the risk for *Bacillus anthracis* from

such incidents is limited, and that the public health response should focus on those persons who were directly exposed by opening or handling letters confirmed to contain anthrax. Cutaneous anthrax is the most likely form of anthrax that could be caused by anthrax-contaminated letters and packages that did not have an obvious aerosolizing device. Given its characteristic clinical presentation and excellent prognosis if recognized early and treated, potential exposures can be managed by observation for the development of a suggestive skin lesion and prompt treatment as clinically needed. Therefore, prophylaxis is <u>not</u> recommended for cutaneous anthrax.

All patients with a skin lesion characteristic of cutaneous anthrax, with or without a known exposure, should be treated presumptively with antibiotics (ciprofloxacin or doxycycline until susceptibilities are known, penicillin or amoxicillin if susceptible) until laboratory testing is completed. If laboratory testing is positive for anthrax, treatment should continue for 14 days.

<u>Presumptive Identification key for *Bacillus anthracis*</u>

- Non-hemolytic
- Non-motile
- Encapsulated (requires India ink to visualize the capsule)
- Gram-positive, spore-forming rod

<u>Gram stain morphology of *B. anthracis*</u>

- Broad, gram-positive rod: 1-1.5 x 3-5 □ occurring singly or in short chains, often with squared off ends
- Oval, central to subterminal spores: 1 x 1.5 □ with no significant swelling of cell
- Spores usually NOT present in clinical specimens unless exposed to atmospheric O_2
- In advanced disease, a gram stain of unspun blood may be positive.

<u>Colonial and Isolate Characteristics of *B. anthracis*</u>

- +After incubation on a blood agar plate for 15-24 hours at 35-37^{o} C, well isolated colonies are 2-5 mm in diameter; heavily inoculated areas may show growth in 6-8 hours
- Gray-white, flat or slightly convex colonies are irregularly round, with edges that slightly undulate, and have "ground glass" appearance
- Often have comma-shaped protrusions from colony edge ("Medusa head" colonies)
- Tenacious consistency (when teased with a loop, stands up like a beaten egg white)
- **Non-hemolytic (weak hemolysis may be observed under areas of confluent growth in aging cultures and should NOT be confused with real •-hemolysis)**
- Non-motile
- Susceptible to gamma phage lysis

The Virginia Department of Health requests immediate reporting to the local health department of any suspected cases of cutaneous, inhalational, gastrointestinal, or central nervous system anthrax. Cases may also be reported to the Office of Epidemiology (daytime number: 804-786-6261; after hours number: 866-820-9611).

Appendix 1: Guidelines for Clinicians Evaluating Suspected Cases of Cutaneous Anthrax

VDH requests immediate reporting of all suspected cases of cutaneous anthrax.

Cutaneous anthrax usually begins as a small papule, progresses to a vesicle in 1-2 days, which ulcerates and forms a black eschar (necrotic ulcer) in 3 to 7 days. The lesion is usually painless and the tissue surrounding the skin lesion is often erythematous, and may have varying degrees of edema. Patients also may have fever, malaise, headache and regional lymphadenopathy. The case fatality for cutaneous anthrax is 20% without and $\leq$ 1% with antibiotic treatment. Cutaneous anthrax is not easily transmissible from person to person, although there is a very low risk of infection if there is direct contact with the drainage from an open sore. The incubation period is usually from 1-7 days, but may range up to 12 days. (Pictures of skin lesions can be found on this web site: www.pighealth.com/Scourse/anthrax.htm)

A highly suspicious case of cutaneous anthrax is:

1 - Any person with a skin lesion meeting the following clinical criteria:

- **An ulcerative lesion with surrounding erythema, edema or vesicles and/or**
- **A blackened eschar**

2 - Any person with a less suspicious skin lesion (i.e. an ulcerative or necrotic lesion), if any of the following are present:

a - a history of working in or having contact with a person who works in a major media establishment, particularly if the patient handles mail

OR

b - a history of exposure to a threatening letter with powder

OR

c - laboratory evidence suggestive of possible *B. anthracis* infection (including gram positive bacilli on gram stain from a skin lesion, sterile fluid, or tissue, or encapsulated non-motile non-hemolytic bacilli on culture from any bodily fluid or site)

All patients with a skin lesion characteristic of cutaneous anthrax, with or without a known exposure, should be treated presumptively with antibiotics until laboratory testing is completed. Ciprofloxacin or doxycycline should be given until susceptibilities are known; if susceptible, penicillin or amoxicillin are acceptable alternatives. If laboratory testing is positive for anthrax, treatment should continue for 14 days.

Instructions for Collecting Laboratory Diagnostic Specimens for Suspected Cases of Cutaneous Anthrax: Laboratory testing at the CDC will be prioritized for highly suspicious cases only (see case definition above). If you have a case that meets these criteria, please contact VDH immediately. We will arrange transport of the diagnostic specimens from your facility to the state laboratory, the Division of Consolidated Laboratory Services.

A. For highly suspicious cases, recommended specimens include:

1. **Obtain two skin biopsies for PCR and immunohistochemical staining:**
    a. One biopsy specimen in formalin, keep at room temperature, for histopathology and immunohistochemical staining. Paraffin-embedded specimens are acceptable as well.
    b. One biopsy specimen in a sterile cup, freeze at –70 C or place on dry ice, for culture and PCR.
2. **Culture and gram stain of skin lesion or skin biopsy for testing at your routine microbiology laboratory:**
    a. Synthetic (non-cotton) swab with non-wooden stick for culture and gram stain of material swabbed from a vesicle or from the border area of the eschar
    b. Biopsy specimen should be sent in sterile saline for culture
    c. Send to routine hospital laboratory, if suspicious *Bacillus* species* is identified, contact VDH immediately.
3. **Acute serum for ELISA testing for *B. anthracis*:** Ideally, within 5 days of illness onset,
    a. collect ~5 ml of whole blood in a serum separator tube, refrigerate or keep at room air
    b. spin down as soon as possible
    c. after spinning, separate serum and freeze the tube of serum at –70 C or place on dry ice
4. **Convalescent serum for ELISA testing for *B. anthracis*:** At 14-21 days after acute sera,
    a. collect ~5 ml of whole blood in a serum separator tube, refrigerate or keep at room air
    b. spin down as soon as possible
    c. after spinning, separate serum and freeze the tube of serum at –70 C or place on dry ice.

If the patient is febrile or hospitalized, please also collect:

5. **Blood culture:**
    Send to routine hospital laboratory, if suspicious *Bacillus* species* is identified, contact VDH immediately
6. **Whole blood for PCR – Use an EDTA containing tube (purple top)**

B. For less suspicious cases, recommended specimens include:
For patients with skin lesions in which cutaneous anthrax is part of the differential diagnosis, but the clinician does not strongly suspect it, and when no potential exposure has occurred and there is no laboratory evidence of infection with a *Bacillus* species, providers may wish to obtain the following specimens.

1. **Culture and gram stain of skin lesion:**
    a. Synthetic (non-cotton) swab with non-wooden stick for culture and gram stain of material swabbed from a vesicle or from the border area of the eschar
    b. Biopsy specimen should be sent in sterile saline for culture
    c. Send to your routine hospital laboratory, if suspicious *Bacillus* species is identified, contact VDH immediately
2. **Blood culture (if patient is hospitalized, febrile, toxic or skin lesion is severely erythematous or edematous):**
    (Send to your routine hospital laboratory, if suspicious *Bacillus* species is identified, contact VDH immediately)
3. **Obtain two skin biopsies for PCR and immunohistochemical staining:**
    (NOTE: The availability of PCR and immunohistochemical staining at CDC may be limited depending on the volume of requests. Therefore, it may be necessary to prioritize testing for patients with more highly suspicious lesions.)
    a. Fresh frozen tissue for gram stain and culture (send to routine hospital laboratory, if suspicious *Bacillus* species is identified, contact VDH immediately)
    b. Formalin-fixed or paraffin-embedded tissue specimens.
    (NOTE: Histopathology is not particularly useful for anthrax)

Please be sure to completely and clearly label all specimens with the following information:

- PATIENTS FIRST AND LAST NAME
- DATE OF BIRTH
- DATE OF COLLECTION OF SPECIMEN
- SITE OF SPECIMEN COLLECTION

* Suspicious *Bacillus* species: Large, Gram positive rods with spores; non-motile and non-hemolytic *Bacillus* species on preliminary culture.